UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/536,841	03/27/2000	Jian-Bing Fan	2825.1016-001	4992

21005 7590 08/08/2003

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER	
WHISENANT, ETHAN C	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

SUPPLEMENTAL **Office Action Summary**	**Application No.** 09/536,841	**Applicant(s)** FAN ET AL.	
	Examiner Ethan Whisenant, Ph.D.	**Art Unit** 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *the telephonic interview held 15 JUL 03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2 and 20-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

SUPPLEMENTAL NON-FINAL OFFICE ACTION

1. The action is made in response to telephonic interview held with the applicant's representative on 15 JUL 03. Please see the attach interview summary. This action is supplemental to and replces the Non-Final Office Action mailed 29 MAY 03.

Claim 2 (3X amended), Claim 20 (2X amended), Claim 21 (2X amended), Claim 21 (2X amended) Claims 23-25 (as originally filed), and Claims 3-19 and 26-40 is/are pending in this application. Claims 3-19 and 26-40 have been withdrawn as the result of a restriction requirement. An action on **Claim(s) 2, and 20-25** follows. Rejections and/or objections not reiterated from the previous office action are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
>
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** The invention was described in –
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)

35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 103

5. **Claim(s) 2 and 20** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugozzoli et al. (1992) in view of Shumaker et al. (1996) and the Stratagene Catalog (1988).

Claim 2 is drawn to an kit comprising three components. First the kit is to comprise an array comprising one or more oligo tags fixed to a solid substrate wherein each oligo tag comprises a unique known arbitrary nucleotide sequence of sufficient length to hybridize to a locus-specific tagged oligo. Next the kit is to comprise, one or more locus–specific tagged oligos which are to comprise a 5' end nucleotide sequence, which hybridizes to the arbitrary sequence of a corresponding oligo tag on the array, and a 3' end nucleotide sequence, complementary to a target polynucleotide sequence in a sample, wherein the last nucleotide at the 3' end of the locus-specific tagged oligo hybridizes exactly one nucleotide before a nucleotide to be queried in the target polynucleotide sequence. Finally, the kit is to comprise at least two labeled ddNTPs, each of which is distinctly labeled. **Claim 20** is drawn to a kit comprising three componets. To begin, the kit is to comprise a pair of primers which are capable of

amplifying a region of dsDNA which region comprises a polymorphic locus. Next, the kit is to comprise an extension primer which extension primer comprises a 3' portion complementary to a portion of the region of dsDNA and a 5' oligonucleotide portion which is not complementary to the region of dsDNA but which is complementary to a unique known sequence of an oligonucleotide tag fixed to a solid substrate, wherein last nucleotide at the 3' end of the extension primer hybridizes exactlly one nucleotide before the polymorphic locus. Finally, the kit is to comprise at least two labelled dd NTPs each of which is distinctly labeled.

Ugozzoli et al. teach a method utilizing the first two components of the kit recited in Claims 2 and 20 along with radiolabeled dNTPs in order to identify specific alleles. Therefore, it can be argued that Ugozzoli et al. teach all of the limitations of Claims 2 and 20 except Ugozzoli et al. do not teach using two or more labeled ddNTPs, each of which is distinctly labeled. However, Shumaker et al. do teach using labeled ddNTPs, each of which is distinctly labeled [i.e. fluorescently labeled with flurophores which result in different fluorescent emissions (i.e. different colors) upon excitation], see, for example p.349. Shumaker et al. also teach multiplexing in an assay very similar in nature to that of Ugozzoli et al. See, for example, 1st Column on page 353.

Note that Ugozzoli et al., while explicitly teaching the amplification and detection of only a single SNP (i.e. the two-allele polymorphism present at codon 192 of the human tyrosinase gene), these authors do teach multiplexing (i.e. the analysis of multiple samples simultaneously) and suggest that such a format could be easily automated. See, for example, the last paragraph on page 107.

In view of these findings and absent an unexpected result, the examiner contends that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to combine the process of Ugozzoli et al. with that of Shumaker et al. The motivation to make the modification recited above would have been to eliminate the need for the radionucleotides of Ugozzoli et al. thereby making the assay of Ugozzoli et al. less dangerous and less expensive to perform.

It is noted that niether Ugozzoli et al. and/or Shumaker et al. teach a kit. However, as evidenced by the Stratagene catalog (1988, p.39) the assembly of a kit with which to perform experiments in molecular biology was routine in the art, and, absent an unexpected result, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to the place the appropriate reagents for performing the methodolgy suggested by Ugozzoli et al. in view of Shumaker et al. into appropriate containers and then package these containers into a kit for the expected benefits of convenience and cost-effectiveness.

6. **Claim(s) 21-24** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugozzoli et al. (1992) in view of Shumaker et al. (1996) and The Stratagene Catalog (1988) as applied against Claim 2 and 20 above and further in view of Reed et al. [US 5,459,038 (1995)].

Claim 21 is drawn to an kit comprising in a single container two or more sets of primers each primer set comprising a pair of primers capable of amplifying a region of dsDNA which region comprises a polymorphic locus. **Claim 22** is drawn to an kit comprising three components all in a single container. To begin the single container is to comprise a set of primers which primers are capable of amplifying a region of dsDNA which region of dsDNA comprises a polymorphic locus. Next the single container is to comprise an extension primer which extension primer coimprises a 3' portion which is complementary to a portion of the region of dsDNA and a 5' portion which is not complementary to the reguion of dsDNA but which is complementary to a unique known sequence of an oligo tag fixed to a solid substrate, wherein 3' end of the extension primer is complementary to the 3' nucleotide sequence of the polymorphic locus and wherein the last nucleotide at the 3' end of the extension hybridizes exactly one nucleotide before the polymorphic locus. Next the single container in the kit is to comprise at least two labeled ddNTPs, each of which is distinctly labeled. Finally, the single container in the kit is to comprise a solid support comprising an attached probe which probe is complementary to the 5' portion of the extension primer .

As argued above Ugozzoli et al. (1992) in view of Shumaker et al. (1996) and The Stratagene Catalog (1988) teach all of the limitations of Claims 21 and 22 except these authors do not teach placing the primer sets in the same container.

Note that Ugozzoli et al., while explicitly teaching the amplification and detection of only a single SNP (i.e. the two-allele polymorphism present at codon 192 of the human tyrosinase gene) Ugozzoli et al. do teach multiplexing (i.e. the analysis of multiple samples simultaneously) and suggest that such a format could be easily automated. See, for example, the last paragraph on page 107. In addition, Shumaker et al. also teach multiplexing (see, for example, Column 1 on page 353) in an assay very similar in nature to that of Ugozzoli et al.

Also note, that Reed et al., teach placing all of the reagents (i.e. primers, dNTPs, polymerase) necessary to carry out a nucleic acid based assay into a single tube in order to improve quality control. See, for example, Column 19 of Reed et al. In addition, Reed et al. teach kits comprising the reagents necessary to carry out nucleic acid based assays. Finally note that Uggololi et al. teach using a solid support comprising an attached probe which probe is complementary to the 5' portion of the extension primer.

In view of these findings and absent an unexpected result, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the kit suggested by

Ugozzoli et al. in view of Shumaker et al. and the Stratagene Catalog wherein two or more primer sets for amplifying multiple polymorphic loci are placed in a single container. The motivation to make the modification recited above would have been to reduce the number of pipetting steps thereby improving quality control.

Likewize, absent an unexpected result, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the kit suggested by Ugozzoli et al. in view of Shumaker et al. and the Stratagene Catalog wherein all of the reagents (i.e. primers extension primer(s), ddNTPs and a solid support comprising an attached probe which probe is complementary to the 5' portion of the extension primer(s) are placed in a single container. The motivation to make the modification recited above would have been to reduce the number of pipetting steps thereby improving quality control as taught by Reed et al.

Claim 23 is drawn to an embodiment of Claim 22 wherein the solid support is an oligonucleotiode array.

Ugozzoli et al. teach this limitation, see for example Figure 1. Note that a single oligonucleotide attached to a solid support is an "oligonucleotide array".

Claim 24 is drawn to an embodiment of Claim 22 wherein solid support is bead. Shumaker et al. teach this limitation, see for example p.347-348, under the heading "Gel-based Assay".

7. **Claim(s) 25** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ugozzoli et al. (1992) in view of Shumaker et al. (1996) and Reed et al. [US 5,459,038 (1995)] as applied above against Claim 22 and further in view of Mitsuhashi et al. [US 6,251,247 (2001)].

Claim 25 is drawn to an embodiment of Claim 22 wherein solid support is a microtiter plate.

Ugozzoli et al. in view of Shumaker et al. the Stratagene Catalog and Reed et al. teach all of the limitations of Claim 25 except these authors do not teach using a microtiter plate as a solid support. However, as evidenced by Mitsuhashi et al. the use of microtiter plates as a solid support for oligonucleotides in nucleic acid based assays was well known in the art at time of the invention. The substitution of one well known reagent with known properties for a second well known reagent with known properties is routine in the art, absent an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their

common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

CONCLUSION

8. **Claim(s) 2 and 20-25** is/are rejected and/or objected to for the reason(s) set forth above.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (703) 308-6567. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached at (703) 308-1152.

The fax number for this Examiner is (703) 746-8465. Before faxing any papers please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989). Any inquiry of a general nature or relating to the status of this application should be directed to the group receptionist whose telephone number is (703) 308-0196.